Hyperparathyroidism in the Elderly

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Primary hyperparathyroidism was studied in a well-defined geriatric population of 1129 individuals during a three-month interval. Primary hyperparathyroidism was diagnosed in 1.5%. The diagnosis was based on a morphologic and biochemic basis. From clinical material consisting of 400 patients treated surgically for primary hyperparathyroidism during a ten-year period, 158 patients (38%) above the age of 64 were studied. At the preoperative evaluation, neuromuscular symptoms were present in 80%, renal insufficiency and kidney stones in each 16%, constipation and/or anorexia in 38%. Ten per cent were considered asymptomatic. In 80% the primary hyperparathyroidism was caused by a solitary adenoma. Ninety-four per cent became normocalcemic following the operation. Consistent hypocalcemia requiring vitamin-D treatment occurred in 3%, and 2% had a persisting hypercalcemia or later recurrence. The therapeutic effect on the neuromuscular symptoms, constipation, anorexia, and renal stone formation was considered good or fair in most of the cases. Primary hyperparathyroidism in the elderly occurs with a high prevalence. It can be treated successfully by surgical therapy with a low cost of morbidity, mortality, and medical care.

PRIMARY HYPERPARATHYROIDISM is diagnosed and treated in an ever-increasing number of patients. Routine screening for S-calcium as well as improved knowledge of the clinical characteristics of the disease are the main reasons for this development. A considerable part of these patients belong to the higher age groups in which autopsy studies indicate that parathyroid adenoma is present in about 7%.[1] The clinical picture of hyperparathyroidism in the aged patient seems to differ markedly from the symptoms and manifestations observed in younger or middle-aged people. This is characterized by mental disturbances which are found in about 50%. These consist of slight or severe neurastenic personality changes, principally depression, acute organic psychosis in most severe cases, or just lack of initiative in most cases.[2] The diffuse psychiatric symptoms usually cannot be distinguished from other manifestations of aging. Frequently, the clinical manifestations of the disease can be estimated more in qualitative terms than in quantitative. The clinical picture of sudden accentuated aging is a common manifestation.[3]

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Submitted for publication: May 26, 1982.

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Also, in advanced ages, hyperparathyroidism is usually a surgically treatable metabolic derangement. The aim of the present investigation is to report a prevalence study of an elderly population and to report some of the clinical experiences with primary hyperparathyroidism in elderly patients during a ten-year period.

Material and Methods

Prevalence Study

The prevalence study was performed during a three-month period at two geriatric hospitals in Malmö, Sweden; 1129 patients, 60 years of age and older, were investigated. Six hundred and ninety-six were hospitalized and 433 were out-patients at the same hospitals. The distribution of the subjects' age and sex is presented in Figure 1. Single or repeated S-calcium determinations were performed in each individual. In the hospitalized group of individuals, a blood sample was taken in the morning before breakfast. In the group of ambulatory individuals, the blood sample was usually not taken under fasting conditions. Hypercalcemia was considered to be present at an S-calcium level of 2.65 mmol/l or more (normal range 2.20–2.60 mmol/l). Individuals who died during the three-month period or later were autopsied.

In addition to hypercalcemia, the diagnosis of hyperparathyroidism was based on one or more of the following three criteria: 1) parathyroid adenoma or hyperplasia at the neck exploration; 2) parathyroid adenoma or hyperplasia at the autopsy; 3) elevated S-PTH level.

The clinical Study

The clinical material consisted of 158 patients who were 65 years of age or older at the time of operation for hyperparathyroidism. They formed the upper age group from a consecutive series of 400 patients surgically treated for primary hyperparathyroidism at the Depart-

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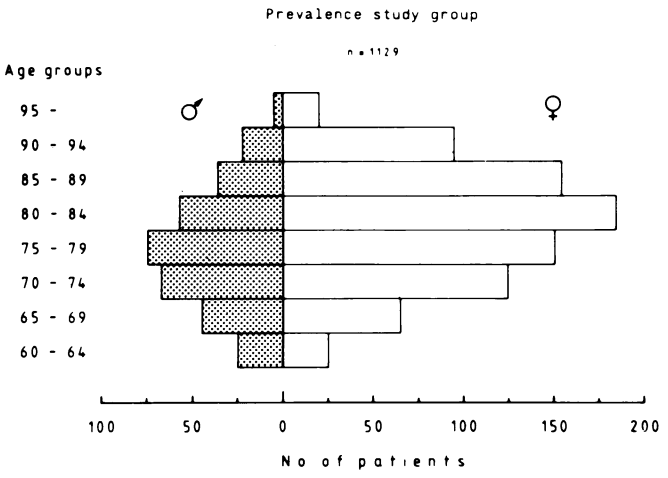

FIG. 1. Geriatric population in which the prevalence of primary hyperparathyroidism was studied.

ments of Surgery, Malmö General Hospital 1971 to 1981 and Lund 1971 to 1974. Preoperative and postoperative evaluations were performed as to clinical signs and symptoms of hyperparathyroidism and the effect of surgical treatment. The age-distribution is depicted in Figure 2. Eighty-six per cent were women. All patients were regularly followed up as to general condition, postoperative sequelae, and S-calcium level. The postoperative observation period ranged from one to six years.

The surgical technique was conventional, implying bioptic verification of normal and pathologic parathyroid tissue intraoperatively. When a single adenoma was present, the diseased gland was removed. In macroscopically multiglandular disease, parathyroid tissue corresponding to one normal gland was left in situ if all four glands were enlarged. Otherwise, enlarged glands were removed and normal glands were biopsied. The

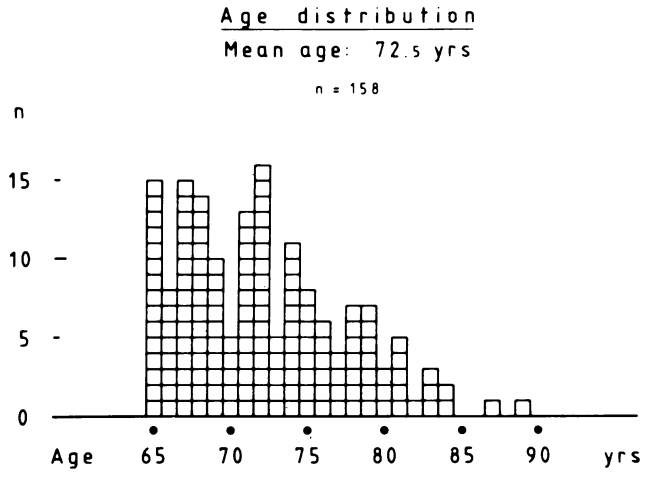

FIG. 2. Age-distribution of 158 patients ≥65 years of age surgically treated for primary hyperparathyroidism.

surgical procedures were performed under general anaesthesia except in one case in which the general condition of the patient did not allow it. This patient was explored under local anesthesia.

Results

The prevalence study

Hypercalcemia was found in 28 individuals (2.5%). The increased S-calcium values varied between 2.65 and 3.25 mmol/l. In the hypercalcemic individuals, the mean value for S-albumin was 42 mmol/l. For 17 patients (1.5%), the diagnostic criteria of hyperparathyroidism were met. In two the histologic diagnosis was obtained at a surgical exploration, in four morphologic diagnosis was obtained at autopsy, and in eleven the diagnosis was based on elevated S-PTH. In each of the six patients with morphologic verification of the diagnosis, a solitary adenoma was present. In six hypercalcemic individuals who did not meet the criteria for hyperparathyroidism, the most likely reason for hypercalcemia was kidney carcinoma, colon carcinoma, malignant lymphoma, breast carcinoma, immobilization from rapidly progressing amyotrophic lateralsclerosis, and, in one patient, thiazid medication. Six of the individuals with hypercalcemia had thiazid medication, but five of these were considered to suffer from hyperparathyroidism. In five individuals the reason for the hypercalcemia could not be identified. Three of these died before S-PTH analysis was performed. At autopsy the parathyroid glands were found to be normal. In one patient a follow-up examination was not possible for other reasons. One patient had a border-line value of S-PTH and is still being followed up. The proportion of females in the investigated population was 71%. Among the hypercalcemic individuals, 85% were women, and among the individuals with hyperparathyroidism, 94% were women. The individuals with proven hyperparathyroidism were evenly distributed between the age of 65 and 92. All 17 diagnoses of hyperparathyroidism were new.

The Clinical Study

The presenting clinical manifestations that resulted in correct diagnosis of hyperparathyroidism at different ages are listed in Table 1.

Hypercalcemia was noted as a side observation at the treatment of other medical conditions in about 40%. The range of S-calcium before operation was 2.65 to 4.30 with a mean value of 2.92 mmol/l. There was no significant difference in the mean S-calcium levels for the different age groups. At the preoperative evaluation, neuromuscular symptoms such as muscular weakness,

mental astenia and fatigue were present in 80%. Renal insufficiency occurred in 16% and kidney stones in 16%. Gastrointestinal symptoms in the form of gastritis or peptic ulcer disease were present in 13%. Constipation and/or anorexia with or without weight loss was noted in 38%. At the preoperative evaluation, 10% were considered asymptomatic.

The surgical finding was a solitary adenoma in 80% of the patients. In the others, multiglandular disease of varying extent was found. Four enlarged glands were present in six patients, three glands in seven, and two glands in 17 patients. Only one enlarged gland showing a histopathologic picture of nodular hyperplasia was found in two patients. In the macroscopically normal-sized glands of these patients, biopsies revealed a similar picture of nodular hyperplasia as found in the enlarged gland.

As a result of the surgical procedure, the S-calcium level returned to normocalcemia in 94% of the patients (Table 2). Three per cent became consistently hypocalcemic requiring permanent vitamin-D treatment. In these patients, subtotal parathyroidectomy of four enlarged glands had been done, leaving parathyroid tissue corresponding to one normal gland in situ. In one of these patients, three enlarged glands had been removed. Two per cent had a persisting hypercalcemia or later a recurrence. In one of these patients, three enlarged glands had been removed. At re-exploration, residual hyperplastic parathyroid tissue could not be identified. In one patient, a mild hypercalcemia remained after removal of three and a half glands. Since significant clinical symptoms were absent, re-exploration was abandoned. All patients who did not become normocalcemic without medication or who had a persisting or recurring hypercalcemia suffered from multiglandular disease and had been operated with subtotal parathyroidectomy. The effect on the neuromuscular symptoms was considered good or fair in most of the cases. These clinical improvements were frequently difficult to evaluate in quantitative terms. Many patients experienced an increased feeling of well-being with less fatigue, improved emotional balance, and an increased interest in their surroundings. A good or fair effect of the operation was also observed in patients with constipation and anorexia. Renal stone formation ceased, but impaired kidney function remained unaffected.

Complications to the surgical treatment occurred in six patients. Unilateral vocal-cord palsy was noted in four patients; in three of them it was transient. The patient with a remaining unilateral vocal cord palsy had been operated previously with a subtotal bilateral thyroidectomy for toxic goiter. Two patients had a postoperative hemorrhage requiring reoperation. No postoperative mortality occurred.

TABLE 1. *Presenting Symptoms in Surgically Verified Hyperparathyroidism at Different Ages*

Symptoms and Signs	<60 Years of Age (n = 74)	≥60 Years of Age (n = 112)	≥70 Years of Age (n = 61)
Neuromuscular	16%	31%	44%
Renal	41%	19%	10%
Hypercalcemic crisis	4%	4%	3%
Gastrointestinal	1%	1%	2%
Skeletal abnormalities	2%	1%	—
Miscellaneous	3%	—	2%
Incidental finding of elevated S-Ca	31%	42%	39%

The mean length for the postoperative hospital stay was 7.4 days. All patients could return to the level of care from which they had arrived. In some patients the care level could even be reduced. Two individuals from the prevalence study underwent a neck exploration for hyperparathyroidism. A solitary adenoma was removed in both these patients. The predominating symptom of fatigue was markedly relieved after operation, and one patient could be nursed at a less requiring level of medical care.

Discussion

Primary hyperparathyroidism, previously considered a rare diagnosis, is nowadays diagnosed in an ever-increasing number of patients. Improved laboratory routines, including screening procedures in combination with a better understanding of the changing clinical picture of hyperparathyroidism, are the reasons behind this. Particularly striking is the increase of diagnosed hyperparathyroidism in the elderly. In autopsy studies,[1] the occurrence of parathyroid adenomas seems to be higher in the older age groups though the material is small and insecure. From clinical prevalence and incidence studies,[4-6] it is obvious that at least clinically manifest hyperparathyroidism is increasing with age. Another striking feature in all frequency studies is the predominance of females in the higher age groups. Also, in the present study a female dominance around 90% was apparent.

The population of the prevalence study is probably not completely representative for a normal population in these age groups since it consists of patients who were hospitalized or attended ambulatory medical service.

Still, the prevalence figure of 1.5% is in fairly good accordance with the data obtained in the study by

TABLE 2. *Postoperative S-Calcium Level (n = 158)*

Normocalcemia without substitution	149 (94%)
Normocalcemia with Vitamin-D	5 (3%)
Persisting hypercalcemia	3 (2%)
Recurring hypercalcemia	1 (1%)

Hunter Heath III et al.[5] These authors studied the annual incidence of primary hyperparathyroidism of a well-defined population. In the corresponding age groups, this figure was 1.54 per mille.

Eleven patients with biochemically verified diagnosis of S-PTH were not explored. The reasons for this varied. Many had advanced manifestations of cerebrovascular disease. In some, the patient or his relatives opposed surgical intervention. Hyperparathyroidism, complicating other medical conditions, is a frequent occurrence within these age groups. It is a difficult task to evaluate the indications for surgical treatment in these patients, but, as a general rule, it should be stressed that elimination of the metabolic disorder of hypercalcemia is preferable also when combined with other severe medical conditions.

The clinical symptomatology of hyperparathyroidism in this group of elderly patients differed from the one in younger age groups. Instead of kidney, bone, and gastrointestinal manifestations, neuromuscular symptoms dominated. The clinical picture was vague including fatigue, decreased intellectual capacity, emotional instability, anorexia, and constipation, *i.e.*, symptoms frequently found in elderly patients. If time relation was taken into account, it was striking how the clinical picture was characterized by sudden onset of accentuated aging. In 40% the elevated S-calcium level was observed as an incidental finding, but at the preoperative evaluation true asymptomatic disease could be found only in 10%. An increased awareness of the particular form of clinical symptomatology in these patients often resulted in a proper clinical diagnosis before operation. In some patients the beneficial effect of the removal of pathologic parathyroid tissue was obvious ex juvantibus.

The preoperative elevation of S-calcium was often considerable. Although some of the patients only had minor elevations, it should be remembered that a generalized aging process may lead to a reduced tolerance to even slight hypercalcemia. Some of these are truely asymptomatic. In these patients a restrictiveness with surgical treatment should be observed. In the present material there was a good correlation between degree of hypercalcemia and severeness of clinical disease. A solitary parathyroid adenoma was present in 80%. These patients exhibited the best response to the surgical procedure as to relief of hypercalcemia and clinical symptoms. Hypocalcemia requiring permanent vitamin-D medication or persisting or recurring disease occurred only in patients who suffered from multiglandular disease of the parathyroid glands. Complications to the surgical treatment were few and of minor importance for the patients. It is noteworthy that no mortality occurred in this material of rather fragile patients. Generalized anesthesia was applied in all but one in whom the parathyroid exploration was done under local anesthesia. The surgical treatment and the postoperative hospital stay could be performed at a low cost. The mean length of the postoperative period was 7.4 days which did not significantly deviate from the average postoperative length of the younger patients which was 5.4 days.

From the present investigation, it can be concluded that hyperparathyroidism is frequently encountered in elderly patients. In these age groups, women predominate. The clinical picture is different from the one found in younger patients since it is characterized by neuromuscular symptoms, often of a rather vague type. Since many of these are found also in a normal aging group of individuals, it is often difficult to give a specific picture of the disease. It is more a question of quantity than quality of symptoms. Hyperparathyroidism in the elderly often manifests as an accentuated aging. Hyperparathyroidism in elderly patients can be treated successfully by surgical therapy with a low cost of morbidity, mortality, and hospital stay.

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